

The National Institute of Mental Health (NIMH) held its 6th Annual Research Roundtable Wednesday, June 19, 2002, at the National Press Club in Washington, DC.

The Roundtable is integral to NIMH's priority-setting process. It provides a critical forum for the Institute to exchange information with interested organizations and groups and to learn the views and concerns of those invested in helping to build a carefully planned research program. The purpose of the Roundtable is to bring together the NIMH Director and staff with consumers, providers of mental health services, family members, research scientists, representatives from advocacy and professional organizations with an interest in mental health, and others.

This year's meeting began with a welcome and presentation by NIMH Acting Director Richard K. Nakamura, Ph.D. Also presenting News from the Frontlines of Research at the meeting were senior NIMH scientific staff including:



- Judith L. Rapoport, M.D., Chief, Child Psychiatry Branch, NIMH Intramural Research Program, who told participants about her research on Brain Tissue Loss in Teens with Schizophrenia;
- Linda S. Brady, Ph.D., Chief, Molecular & Cellular Neuroscience Research Branch, Division of Neuroscience and Basic Behavioral Science, NIMH, who discussed genetics of anxiety disorders;
- Doreen S. Koretz, Ph.D., Associate Director for Prevention, NIMH, who presented the Promise of Prevention; and
- Ellen L. Stover, Ph.D., Director, Division of Mental Disorders, Behavioral Disorders & AIDS, NIMH, who reviewed the Institute's latest efforts in epidemiology research.

Following a break that gave participants an opportunity to interact with each other and with NIMH staff, the Roundtable reconvened and additional NIMH staff presented selected priorities:

- Ernest Márquez, Ph.D. the new Director, Office of Special Populations, NIMH, was introduced to the Roundtable and discussed priorities for reducing health disparities;
- Wayne Fenton, M.D. Acting Deputy Director of NIMH, told the Roundtable about the Institute's fresh focus on developing new treatments; and finally
- Junius J. Gonzales, M.D., Chief, Services Research and Clinical Epidemiology Branch in NIMH's Division of Services and Intervention Research, demonstrated the Institute's commitment to services research--past, present, and future.

The last hour of the meeting was devoted to open discussion.

National Institute of Mental Health
6th Annual Research Roundtable
 The National Press Club
 529 14th St. NW, 13th Floor - Washington, DC 20045

Wednesday, June 19, 2002

8:00 - 8:30 am **Continental Breakfast**

8:30 - 9:10 am **Welcome and State of the NIMH**---Richard K. Nakamura, Ph.D., Acting Director, NIMH

Questions and Answers

9:10 - 10:30 am **Panel: News from the Frontlines of Research** with Questions from Attendees

- Brain Tissue Loss in Teens with Schizophrenia---Judith L. Rapoport, M.D., Chief, Child Psychiatry Branch, NIMH Intramural Research Program
- Using Genetic Turn-Ons and Turn Offs to Understand Anxiety---Linda S. Brady, Ph.D., Chief, Molecular & Cellular Neuroscience Research Branch, Division of Neuroscience and Basic Behavioral Science, NIMH
- The Promise of Prevention---Doreen S. Koretz, Ph.D., Associate Director for Prevention, NIMH
- Mental Health of America: A New Accounting---Ellen L. Stover, Ph.D., Director, Division of Mental Disorders, Behavioral Disorders & AIDS, NIMH

10:30 - 11:00 am **Break and Refreshments**

11:00 am - 12:00 pm **Selected Priorities**

- Priorities for Reducing Health Disparities---Ernest Márquez, Ph.D., Director, Office of Special Populations, NIMH
- Developing New Treatments---Wayne Fenton, M.D., Acting Deputy Director, NIMH
- NIMH Services Research: Past, Present, Future---Junius J. Gonzales, M.D., Chief, Services Research and Clinical Epidemiology Branch, Division of Services and Intervention Research, NIMH

12:00 - 1:00 pm **Open Discussion**

DIRECTOR'S REPORT

The Public Health Mission of NIMH

Dr. Richard Nakamura opened the meeting by describing the significant public health



mission of the NIMH, which is to reduce the burden of mental illness and behavioral disorders through research on mind, brain and behavior. NIMH is one of 27 Institutes and Centers that make up the National Institutes of Health (NIH), the nation's premier biomedical research agency. NIH is one of eight health agencies that are part of the U.S. Department of Health and Human Services. NIH's primary tasks are to perform and to fund research, most of which is conducted by scientists and physicians at universities, hospitals, and clinics across the Nation. In addition, Congress has directed NIH to support information and education programs about mental illness and mental health.

NIMH's public health mission is made even more significant given the burden of mental illnesses, both to the individuals and to our society as a whole. The World Health Organization, the World Bank, and Harvard University authored the revolutionary Global Burden of Disease Study that found of the 10 leading causes of disability in the U.S. and other developed countries, four are mental disorders: major depression, bipolar disorder, schizophrenia, and obsessive-compulsive disorder. While mental illnesses are responsible for slightly more than one percent of death, they account for almost 11 percent of disability worldwide. In developed nations major depression is second only to heart disease in life-years lost from illness. By 2020, it is expected to be the second leading cause of disability in the world. Mental illnesses including suicide account for 15% of the overall burden from disease, putting them on par with cancer and heart disease, which is staggering.

Dr. Nakamura told the Roundtable about NIMH-grantee Ronald Kessler's recent research in epidemiology. Dr. Kessler revealed some preliminary findings to Dr. Nakamura that underscore the seriousness of our mission. The discussion between them began over a Gallup Poll that asked a representative sample of Americans about their days lost from work due to bodily or mental illnesses. The press reported that the poll indicated that bodily illnesses cause more lost days than mental illnesses, because two thirds of the days were taken due to general medical illnesses. However, the extraordinary story that went unreported was that fully 30% of the days were lost due to mental illnesses. Dr. Nakamura asked Dr. Kessler what his data are showing and he reported that 20-25% of job performance loss is attributable to mental illnesses.

To meet this burden, NIMH's total research budget, including information outreach, is approximately \$1.2 billion per year. Dr. Nakamura thanked the President and Congress for doubling the NIH budget, which has enabled the Institute to fund more worthy projects. NIMH is the 8th largest institute at NIH and currently is able to fund 25-30% of the reviewed applications it receives. They are chosen through a highly competitive, rigorous process to ensure that research of the highest quality and greatest scientific opportunity is funded.

A Challenging Year

The horrific events of September 11th, financial uncertainties, the departure of Steve Hyman, M.D. as director of NIMH, as well as similar vacancies in sister institutes, and an overburdened U.S. mental health care system have made this a challenging year for the Institute.

September 11, 2001. Following the terrorist attack on the World Trade Center and the Pentagon, there was an outpouring of volunteerism from the NIMH staff. Organized by Dr. Wayne Fenton, now Acting Deputy Director of the Institute, 40 outstanding clinicians from NIMH responded as the entire country reached out. Although these volunteers were not needed on site, NIMH organized an effort to teach clinicians who were dealing with the aftermath what to expect and how to recognize and treat the mental health problems they would likely see. As it turned out, NIMH had planned a meeting on trauma care for the very week following September 11th. Since the invitees were unable

to travel and the effort was deemed crucial the meeting was turned into a conference call. NIMH played a critical role in responding to the anxieties inherent in attacks as well. Former NIMH Director, Dr. Steven Hyman briefed the public and Members of Congress and their staffs in the aftermath of the anthrax attacks to explain the terror in bioterror. NIMH scientists explained what we knew about post-traumatic stress disorder (PTSD) and focused on what the press was reporting. NIMH pointed out that the constant repetition of the frightening images from that day was not helping the Nation to heal, but instead was increasing stress and PTSD symptoms. And in late October, at a Grand Rounds presentation at NIH, Dr. Anthony Fauci (Director of NIAID) and Dr. Hyman discussed the anthrax outbreak and addressed the physiology and psychology of terrorism.

If there was a silver lining after these terrible events, it was that after September 11th there was general recognition that strong individuals heroes, firemen, and policemen could be expected to develop mental illnesses, and it could happen to all "normal" Americans.

During his tenure (1996-2001), Dr. Hyman made profound changes at the Institute: the entire structure was revamped, the research focus sharpened onto causes and cures. These changes made the Institute stronger and left it in a better position to carry on after his departure to become Provost at Harvard University in December. Dr. Nakamura told the Roundtable that the National Advisory Mental Health Council (NAMHC) meeting in January 2002 went very well. The Council was forward thinking, excited and enthused about the promise of the future and very supportive of his interim directorship. Dr. Nakamura said that NIMH is in the midst of a search for a new director, and judging from the group of outstanding people who have applied for the position, NIMH's new leader will be exceptional.

Dr. Nakamura also indicated that he has contacted many other agencies to set up liaisons and in particular created an "Acting Directors" group, made up of the Directors of the NIMH, the National Institute of Neurological Disorders and Stroke, the National Institute on Drug Abuse (NIDA), and the National Institute on Alcohol Abuse and Alcoholism (NIAAA) that meets every other week. The Institute is working well with the Department of Health and Human Services (HHS) also, particularly the Substance Abuse and Mental Health Services Administration (SAMHSA). Dr. Nakamura described the unfortunate bitterness following the reorganization of the Alcohol Abuse and Mental Health Administration, during which NIMH, NIAAA and NIDA returned to the NIH, as the typical by-product of a divorce. He said that former Surgeon General David Satcher played an important role in healing the wounds. Since Charles Curie's appointment as Administrator of SAMHSA, a renewed attention has been paid to the link between research and services and there has been new and ongoing interaction between SAMHSA and the former Alcohol, Drug Abuse, and Mental Health Administration institutes. The Institute has also continued to forge links with the Justice Department to help stop criminalization of mental illnesses and with the Department of Defense, which has a serious interest in maintaining a military that is mentally healthy. In recognition that mental illnesses are often worse for children, NIMH staff have also connected with Department of Education staff to see what can be done during development to avoid losing these children altogether.

At the House Appropriations hearings this spring, there were six panels of institutes. Although NIMH was on the panel addressing training and infrastructure, in his testimony, Dr. Nakamura showed the Members of the Subcommittee how neurogenesis occurs throughout life, which captured their attention. Representative Patrick Kennedy also kept a focus on mental health and illnesses in the hearing.

Planning for the Future

NIMH has made great strides in planning for the future. *Breaking Ground, Breaking Through: The Strategic Plan for Mood Disorders Research* that the Roundtable first heard about at last year's meeting has been completed and, in fact, the first advance copies of the Executive Summary were made available to attendees. The complete plan will be printed in the September issue of *Biological Psychiatry*. The public was invited to read the plan and make comments via the website prior to publication.

Dr. Nakamura noted that later in the morning the Roundtable would hear from Dr. Wayne Fenton discussing the Institute's new emphasis on developing novel treatments. There is an urgent need to translate findings in basic neuroscience, genetics, and basic behavioral science into diverse clinical applications: novel treatments, diagnostic tools, epidemiologic approaches that could lead to preventive interventions, and surrogate markers for clinical trials. In a major new enhancement of treatment improvement research, NIMH is planning to launch, in FY 2003, a sweeping initiative designed to introduce fundamentally new approaches to the development of treatments for mental disorders.

Dr. Nakamura announced personnel changes, including Dr. Ernest Márquez the new Director of the Office of Special Populations, also on the agenda; Dr. Eve Moscicki who is Acting Director of Child and Adolescent Mental Health Research and Chair of the Child Consortium; and Dr. Jason Olin who is the new head of the Institute's Aging Consortium.

Dr. Nakamura also remarked on NIMH's specific attention to autism studies, borderline personality disorder and an anxiety disorders initiative. However, he said that none of these activities would be a success without investigators to carry out the research, so NIMH is focusing on training initiatives. It is first necessary to deal with the barriers inherent in clinician training programs that make a research track difficult. NIMH is working with Departments of Psychiatry, the Institute of Medicine, and professional organizations to free up a training track for research and the Institute has eagerly begun to use the loan repayment authority recently granted by Congress. These efforts are vital and a major priority for NIMH.

Recently, the Nobel prizes awarded to Paul Greengard and Eric Kandel, both of whom were funded by NIMH for over 30 years each, spotlighted the importance of longterm support for basic research. We've been reminded that basic research can seem tangential yet it can be crucial. In a recent speech, Greengard talked about what goes on inside a single neuron. For thirty years he has examined synapses and postsynaptic activity. His exciting story illustrated how his pursuit of this inquiry revealed new points for intervention that have been recognized by pharmaceutical companies as potential targets. Similarly Eric Kandel has worked with a seemingly unimportant, simple animal the sea slug. Dr. Kandel wanted to be a psychoanalyst and thought he should try to know something about the brain first. He moved from humans into this much simpler animal to discover the neural basis of behavior. The sea slug [*Aplysia californicus*] has neurons that can be counted and defined. Once identified, one can see how they participate in behavior. From there, he moved on to the mouse and genetically manipulated behaviors. Now he is applying what he learned to humans. Understanding how we lay down memories is one important finding, but this is fundamental knowledge about who we are, and our moods and anxieties. These paths of discovery are vistas that open up rapidly. Basic research in neuroscience will lead to enormous progress, however, we must never forget that people are ill today, they need help today, and clinicians need treatments to use today.

Clinical trials grow out of this fundamental understanding. It is rare that a disorder is "pure" such as depression without substance abuse or suicidal ideation. They are also not limited to any age group. Therefore, NIMH has structured its most recent clinical trials to examine different treatments and

how they will work for people who live in the community perhaps not fitting the strict criteria necessary for participating in traditional clinical trials: We have begun to move away from active ingredient placebo-controlled trials in order to focus on what is the combination of drugs and psychotherapies that will work for particular individuals. While these have their place, our model allows an individual who becomes ill in a trial condition to move on to another treatment and remain in the trial. Our consumers/trial participants get "numerous bites at the apple," even when treatment is not the **primary** focus of the trial.

Another important part of NIMH's work is stigma reduction; and its efforts in conjunction with those of the Roundtable partners have made a difference. Mental illnesses are increasingly recognized as real, diagnosable, treatable sicknesses and people get well. Dr. Nakamura told the Roundtable that members of his own family have bipolar disorder. His grandfather committed suicide and three others of that generation have been diagnosed with the disease. Yet, he did not learn that there was anything different about his family until he had graduated from college. Stigma prevented such knowledge. Now he and his 14 cousins all talk about what can be done to reduce the risks for the next generation. They know already that there will be cases among the children, but the atmosphere is different: You can be treated; you can have a life.

Dr. Nakamura expressed his delight at President Bush's recent interest in mental illnesses. He is genuinely interested and believes that mental illnesses are real and treatable. On April 29 he declared that he is in favor of parity for mental illness insurance coverage. He also announced the formation of the New Freedom Commission on Mental Health, which began meeting June 18. The Commission is charged with conducting a comprehensive study of the United States mental health services delivery system, and advising the President on methods to improve the system. The Commission will identify the needs of people with mental illness, the barriers to care, and investigate communitybased care models that have been successful in coordinating and providing mental health services. The Commission will have one year to recommend improvements that can be implemented by all aspects of public and private mental health systems to improve coordination and quality of services. Michael F. Hogan, Ph.D., Director, Ohio Department of Mental Health and former NAMHC member is the chair. Dr. Elias Zerhouni, the new Director of NIH, was appointed ex officio member of the Commission and he delegated this post to Dr. Nakamura.

Dr. Nakamura expressed his view that Dr. Zerhouni will be especially focused on management of NIH, using private sector criteria to evaluate the efficiency of NIH activities.

Dr. Nakamura continued by thanking the staff for their support of his acting directorship. He said they are the embodiment of caring and effective federal employees. He also thanked the Roundtable partners for their interest, continuing prodding, and support.

Attendees thanked Dr. Nakamura for his leadership over the past six months.

NEWS FROM THE FRONTIERS OF RESEARCH

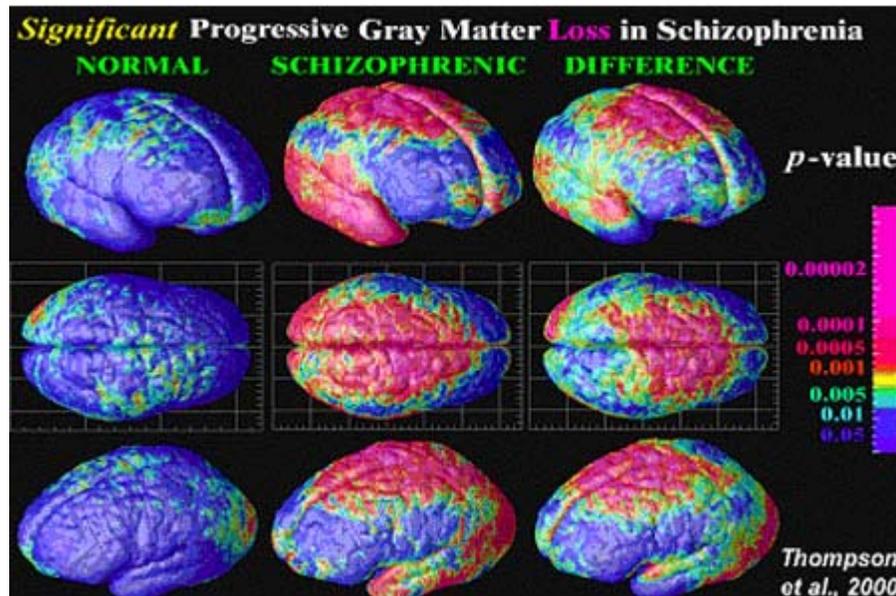
Brain Tissue Loss in Teens with Schizophrenia

Judith L. Rapoport, M.D., Chief, Child Psychiatry Branch, NIMH
Intramural Research Program (IRP)

Dr. Rapoport told the Roundtable partners about her research in the NIMH IRP on children with early-onset schizophrenia. This is an



extremely rare disease. Of 1000 children referred to them as possible candidates for their research, only 65 were actual cases. One reason for studying such children is that they are much sicker at this younger age and the researchers can analyze what happens to them as they grow. They are studying them longitudinally and have found ventricular loss and loss of gray matter. The progression is substantial over time and moves in a characteristic pattern from the back to the front of the brain.



The slide shows brain scans of normal brains versus brains of young children with childhood onset schizophrenia. The scans reveal significant gray matter loss. Brain volume (gray matter) decreases and lateral ventricular volume increases.

Dr. Rapoport showed a "movie" in QuickTime format of the gray matter loss, which could be a focus of treatment. She also showed slides comparing youngsters with bipolar disorder who had been receiving the same antipsychotic treatments as the children with schizophrenia. These children did not show the characteristic pattern of loss, indicating that this pattern was due to the schizophrenia and not a function of the medication. Their most intriguing avenue of inquiry is the examination of siblings, which could lead to the finding of a trait marker because this back to front wave of gray matter loss could be diagnostically specific. The loss stops in early adulthood.

The animation shows that the loss is progressive and moves in a characteristic wave pattern from back to front over time.

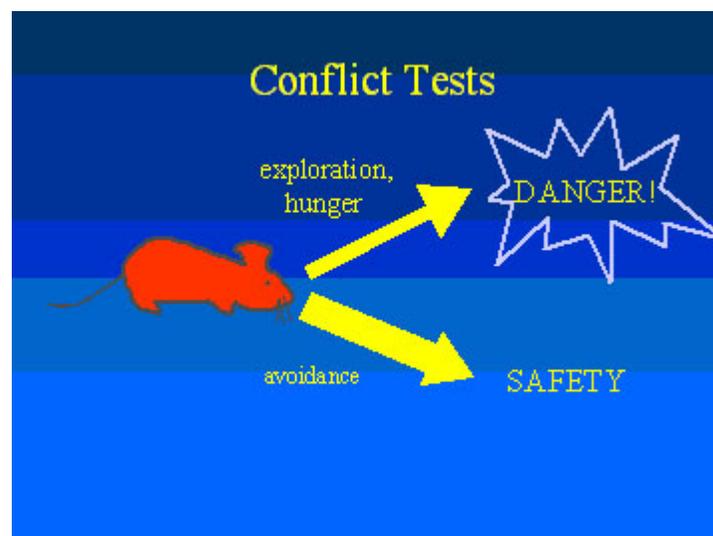
Using Genetic Turn-Ons and Turn-Offs to Understand Anxiety

Linda S. Brady, Ph.D., Chief, Molecular & Cellular Neuroscience Research Branch, Division of Neuroscience and Basic Behavioral Science, NIMH

Dr. Brady's talk centered on genetic approaches used by NIMH-funded

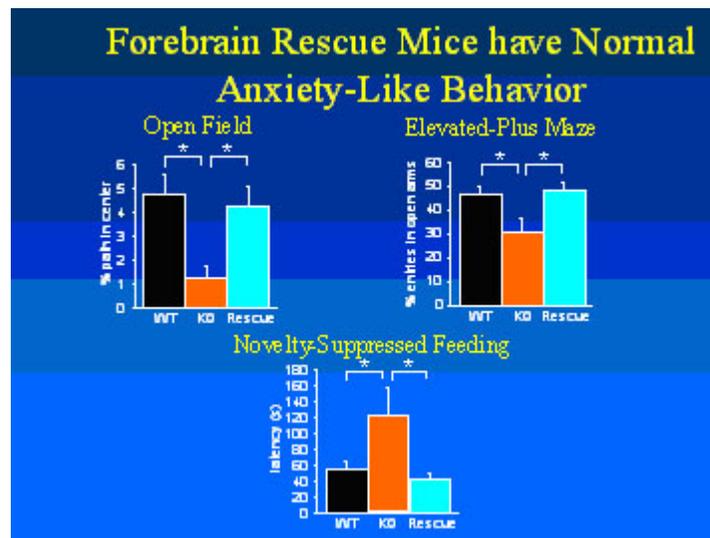


investigators to understand the serotonergic system and mood and anxiety disorders through an animal model. Mood and anxiety disorders are common. Serotonin is implicated in mood regulation and drugs that act on the serotonergic system, such as selective serotonin reuptake inhibitors [SSRIs], are an effective and standard treatment. There are both genetic and environmental factors involved in producing these disorders. A genetic knockout mouse that lacks specific serotonin receptors and shows increased anxiety-like behaviors is being used in this research. Compared to the wild type, the knockout animal behaves in an anxious, defensive manner. A normal mouse needs to explore its world to find food; the knockout mouse avoids open spaces seeking safety.



The slide is a cartoon of conflict tests in which an anxious mouse seeks safety rather than exploring its environment for food.

The researchers determined that expression of serotonin in the forebrain [hippocampus and cortex] is important to reducing this pattern of anxiety since a "rescue" genetic manipulation that restores the serotonin receptor in these brain regions also restores normal behavior. They went on to determine that receptor expression during the early postnatal period, but not in adults, was necessary for this behavioral rescue.



This slide shows bar graphs that compare wild type, knockout, and rescue mice in three trials: open field, elevated plus maze and a type of feeding. In these trials the genetic "rescue" mice performed similarly to the wild type and not in the abnormal way displayed by the knockout mice.

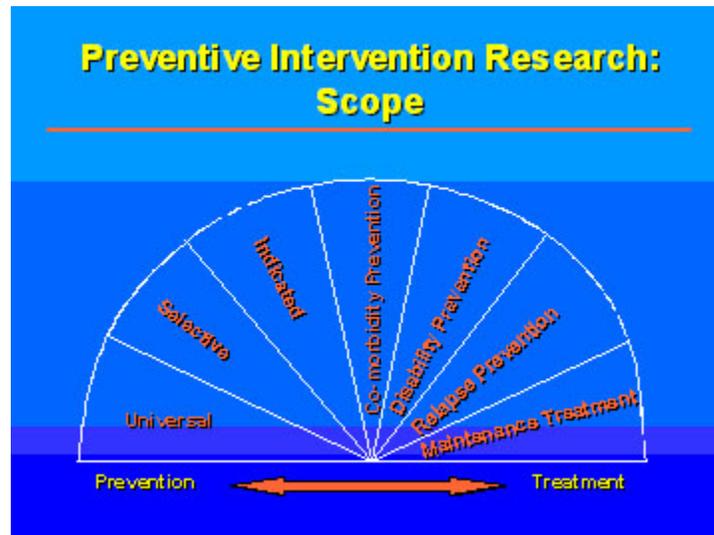
These findings complement results of clinical studies and PET imaging and together suggest that serotonin receptors play a key role in the development of normal emotional behavior and its expression in adulthood. Also genetic knockout and "rescue" technology can be used to understand the pathophysiology of mental disorders and identify targets for drug discovery. In this way, neuroscience can also help us study how the interaction between genetics and the environment works to construct the brain.

The Promise of Prevention

Doreen S. Koretz, Ph.D., Associate Director for Prevention, NIMH

Dr. Koretz began her talk by describing how NIMH views the scope of prevention research.

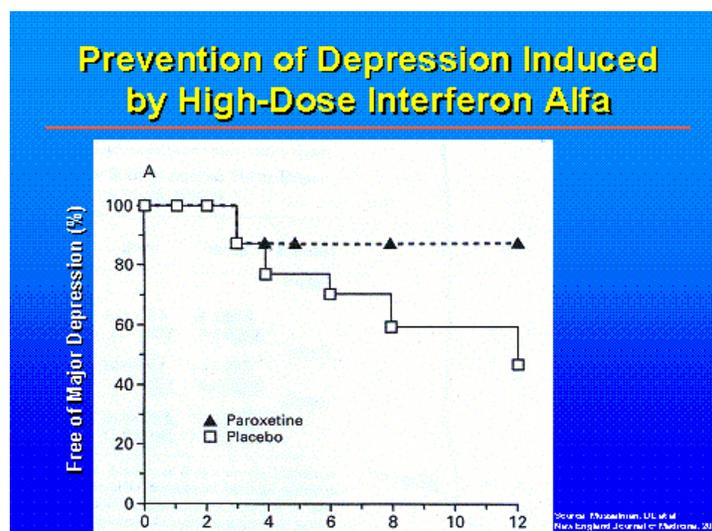




This slide illustrates the scope of preventive intervention research with a half circle divided into pie slices. Each slice shows a research area where an opportunity for preventive intervention exists, from universal prevention (used for everyone) to selective intervention (typically for at-risk populations) to indicated (for people showing symptoms) to comorbidity prevention, disability prevention, relapse prevention, and finally maintenance treatment.

Prevention research extends from preintervention to risk/protective factors research and on to intervention development and testing. Prevention intervention research can take place in different populations: asymptomatic, population based; asymptomatic, highrisk; asymptomatic, previously diagnosed; symptomatic, subclinical, never met diagnostic criteria; symptomatic, previously but not currently diagnosed; or diagnosed. Dr. Koretz described where we are now in prevention studies, indicating that there are promising interventions that are becoming user and policy friendly.

Finally, she presented a study that illustrated the title of her talk: *The Promise of Prevention*. High-dose interferon is being widely used to stop the advance of certain cancers and hepatitis C. An unfortunate sideeffect of the treatment is severe depression and people often abandon their treatment because of it. In order to prevent depression from developing, the study dispensed paroxetine prior to administration of interferon. The results were positive: approximately 90% of those persons receiving paroxetine remained free of depression 12 weeks into treatment, while 50% of those taking placebo succumbed to interferon-induced depression. We have come a long way from the idea, "of course you are depressed, you have cancer." We have learned that depression is not necessary and when prevented, people may continue their treatments and hopefully get better.



This slide is a graphic that displays how depression was prevented in people receiving high-dose interferon alfa. The x-axis is time going out to 12 weeks while the y-axis is the percent of people remaining depression free. Paroxetine prevented depression in 90% of those taking it for 12 weeks. For those taking placebo only 50% were still free of depression at 12 weeks. [Source: Musselman, DL et al, *New England Journal of Medicine*, 2001]

Mental Health Epidemiology -- A New Accounting

Ellen Stover, Ph.D., Director, Division of Mental Disorders, Behavioral Disorders & AIDS, NIMH

Dr. Stover began with a list of reasons why NIMH supports epidemiology research. First, it can help in identifying the causes of mental disorders and factors that increase risk for disorder. Such research can also aid in determining the extent of disorders in a community or our Nation, and can provide insight into the natural history and prognosis of mental disorders. In addition, it can assist in evaluating existing and new preventive and therapeutic measures and modes of health care delivery. Finally, epidemiology research can provide an important foundation for developing public health policy (e.g., mental health parity).



NIMH funded a total of 91 epidemiology studies in FY 2001, many of which are ongoing, including 3 interrelated largescale cooperative psychiatric epidemiology studies: the National Comorbidity Survey (NCS) replication led by Ronald Kessler (Harvard); the National Survey of African Americans (NSAA) led by James Jackson (U. of Michigan); and the National Latino and Asian American Survey (NLAAS) headed by Margarita Alegria (Harvard) and David Takeuchi (U. of Washington, Seattle). A nationally representative sample of 35,000 adults and adolescents is participating. The findings will be compatible with similar research being conducted by the World Health Organization. Some initial results will be released in 2003, and all data should be collected and released by 2005. The study makes an extra effort to sample underserved populations such as

children and the elderly. It is also symptom-based and not diagnosis specific, permitting a major focus on disability.

Dr. Stover presented a slide from Dr. Kessler's work that showed that 3 of the top 10 conditions causing impairments at work are mental disorders.

Ten Leading Causes of Role Impairment Days, U.S. Household Population 1997

Rank	Condition	Mean Monthly Impairment Days
1	Cancer	10.9
2	Heart disease	6.6
3	Ulcer	5.8
4	Generalized anxiety disorder	5.5
5	Panic	5.1
6	Major depression	4.3
7	Arthritis	4.0
8	High blood pressure	3.9
9	Diabetes	3.6
10	Asthma	3.0

Kessler et al. (2001)

The slide is a chart showing the 10 leading causes of role impairment days, U.S. household population 1997. Mental illnesses are 3 of the top 10, ahead of high blood pressure and diabetes. [Source: Kessler, et. al. 2001]

Current NIMH epidemiology research builds on a body of important prior findings, including that of very high rates of comorbidity for both mental disorders and substance abuse.

Lifetime Prevalence with Comorbidity

Disorder	Lifetime Prevalence	Proportion with Lifetime Comorbidity
GAD	5.2%	91.3%
Panic	3.6%	92.2%
PTSD	7.6%	81.0%
Major Depression	17.2%	83.1%
Alcohol Dependence	14.2%	80.6%
Drug Dependence	7.7%	95.7%

Source: Hasler et al. (1998)

This slide is a chart of lifetime prevalence with comorbidity. [Source: Kessler, et. al. 2001]

Another consistent and challenging finding is that although approximately 28% of U.S. adults have mental health/addictive disorders, only 15% use mental health/addictive disorder services. Less than half of these services are provided in specialty mental health settings.

Dr. Stover told the Roundtable how NIMH enhances understanding of the distribution of mental disorders in younger populations through collaborations with the national surveys of other Federal agencies, such as the National Health and Nutrition Examination Survey (NHANESIV), the National Health Interview Survey (NHIS), and the Early Childhood Longitudinal Study Birth Cohort (ECLSB). She explained how a third aspect of NIMH epidemiology research analytic studies could contribute to the increasing body of knowledge about mental illnesses in America. Analytic studies examine how the potency, timing, and sequencing of risk and protective factors interact. Such studies also are advancing our knowledge about mental disorders through the identification of biological and contextual risk and protective factors and targets for prevention and early intervention. Dr. Stover said that future directions for NIMH epidemiology research include: improving child assessment; strengthening links between epidemiology, genetics, developmental sciences and prevention; and informing and improving diagnosis and nosology. She also said that a request for applications or a program announcement would soon be issued that includes a general effort to improve measurement of disorder symptoms and outcomes, an effort that will require the contributions of the behavioral science research community.

SELECTED PRIORITIES

Priorities for Reducing Health Disparities

Ernest Márquez, Ph.D., Director, Office of Special Populations (OSP), NIMH

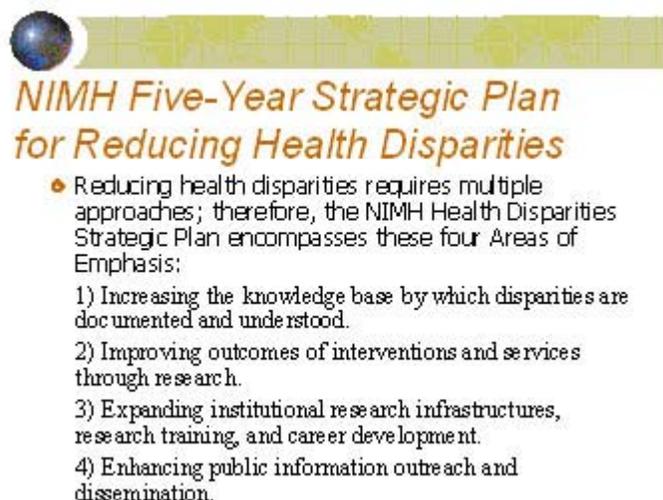
Dr. Ernest Márquez began his talk by reviewing the documents and principles that guide NIMH research priorities for reducing health disparities. These include:

- Mental Health: Culture, Race and Ethnicity (A Supplement to Mental Health: A Report of the Surgeon General)
- NIMH Five-Year Strategic Plan for Reducing Health Disparities
- National Advisory Mental Health Council Workgroup Report entitled "Racial and Ethnic Diversity in Mental Health Research Career"



The main findings of the Surgeon General's supplement on mental health, culture, race and ethnicity are (1) mental illnesses are real, disabling conditions that affect all populations, regardless of race or ethnicity; (2) striking disparities in mental health care are found for racial and ethnic minorities; and (3) minorities are underrepresented in mental health research. Minorities have less access to, and availability of, mental health services and are less likely to receive needed mental health services. Minorities in treatment often receive a poorer quality of mental health care. Dr. Márquez told the Roundtable that "Culture Counts." Living in poverty has the most measurable effect on the rates of mental illness. People in the lowest socioeconomic status are about two to three times more likely than those in the highest strata to have a mental disorder. Racism and discrimination are stressful events that adversely affect health and mental health. Mistrust of mental health services is an important reason deterring minorities from seeking treatment. These concerns are reinforced by evidence, both direct and indirect, of clinician bias and stereotyping. The cultures of racial and ethnic minorities alter the types of mental health services they need. Clinical environments that do not respect, or are incompatible with, the cultures of the people they serve may deter minorities from

using services and receiving appropriate care. Dr. Márquez showed a slide that presented four areas of emphasis of the NIMH Five-Year Strategic Plan for Reducing Health Disparities.

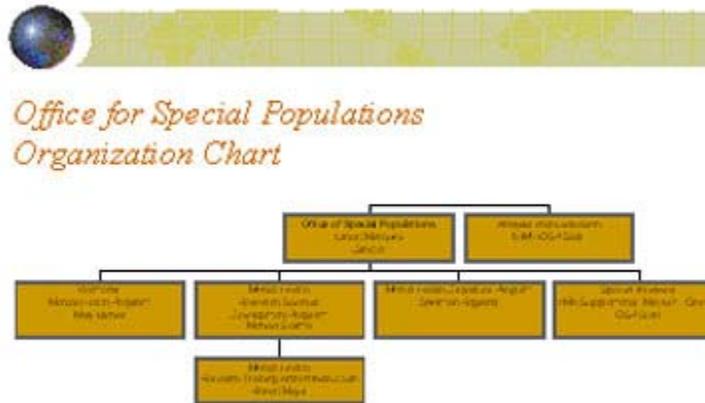
The slide features a title in orange text, a bulleted point, and a numbered list. The background is a light green grid with a globe icon on the left.

**NIMH Five-Year Strategic Plan
for Reducing Health Disparities**

- Reducing health disparities requires multiple approaches; therefore, the NIMH Health Disparities Strategic Plan encompasses these four Areas of Emphasis:
 - 1) Increasing the knowledge base by which disparities are documented and understood.
 - 2) Improving outcomes of interventions and services through research.
 - 3) Expanding institutional research infrastructures, research training, and career development.
 - 4) Enhancing public information outreach and dissemination.

The NAMHC Workgroup Report on Racial and Ethnic Diversity in Mental Health Research Careers also made some excellent recommendations: (1) create a tracking system to monitor the career progression of NIMH-supported trainees through the investigator level so training can be optimized based on outcomes; (2) establish a national mental health research mentorship program devoted to training racial/ethnic minority investigators; (3) concentrate more new resources at the later stages (post-doctoral and beyond) of career development; and (4) encourage new and strengthen existing networks and partnerships to enhance science training goals that exceed NIMH resource capabilities. Furthermore, NIMH is encouraged to a) ascertain that Initial Review Group memberships are diverse and, where relevant, possess the expertise needed to evaluate research in minority populations/communities; and b) enforce sanctions for programs that fail to attract racial/ethnic minority trainees when such criteria are stipulated in the funding mechanisms. Finally, the Workgroup encouraged NIMH to conduct an annual review of plans for racial/ethnic diversity in mental health research careers and of the strategic plan for reducing health disparities to assess progress made in implementing the action plans. NIMH should then report its findings to the NAMHC.

Dr. Márquez showed how the Office of Special Populations is organized to accomplish these mandates.



[Click here for larger image](#)

This slide shows the organization chart of the Office of Special Populations. Dr. Ernest Márquez is the director, Dr. Mary Blehar directs the Women's Program, Dr. Michael Sesma heads the Mental Health Research Scientist Development Program, Robert Mays leads the Mental Health Research Training and Infrastructure efforts, and Mr. Sherman Ragland directs the Mental Health Disparities Program.

The staff are performing outreach, forming partnerships by cooperation and leveraging with the NIMH Extramural and Intramural programs and Research Divisions, the NIMH Extramural Research Community and other NIH Institutes and Centers, other Federal Agencies, professional Societies, and making active partners of the research community/communitybased mental health organizations. Activities also include facilitating information dissemination, outreach to minorities to encourage clinical trial participation, enhancing public information, outreach and dissemination through professional societies, and visits to professional society meetings.

In response to the Workgroup recommendations with regard to training, OSP staff is working to:

- Create a trainee tracking system
- Establish a mentorship program
- Concentrate resources at the later stages of development of mental health researchers
- Encourage new/existing networks/partnership to enhance science-training goals that exceed NIMH resource capabilities
- Initiate efforts to establish Minority and Majority Institutions Partnerships
- Examine and evaluate mechanisms to strengthen Minority Institutional Infrastructure Development
- Develop and augment training and career development opportunities for women & underrepresented minorities in NIMH intramural laboratories
- Develop training programs for women and underrepresented researchers to become proficient in "grantsmanship"
- Establish a continuum of training from Ph.D. through post-doc to faculty member in mental

health research

- Evaluate outcomes of existing training programs (non-minority, minority and women).

Developing New Treatments

Wayne Fenton, M.D., Acting Deputy Director, NIMH



Dr. Fenton told the attendees about an NIMH initiative to develop new treatments for depression and schizophrenia; both medications and psychosocial and behavioral treatments. Why do we need a treatment development initiative? While there have been advances in medications over the years, there are serious limitations in our current treatments. It is a decidedly mixed picture. In depression, for example, 10-20% of patients in trials discontinue due to side effects. Of those who complete the trial, 50-55% respond to target medication within 12 weeks (50% reduction in HAM-D score); however, many who respond have residual symptoms (i.e., chronic underlying depression and high risk for relapse). Complete remission occurs in less than 45% of persons in these trials. Such poor outcomes under the best conditions call to mind the difficulties people with depression are experiencing in their everyday treatment experiences.

Dr. Fenton also told the Roundtable that the outcomes for people diagnosed with schizophrenia also have not greatly improved. Except for a change for the better in the 1960s and 1970s due to new drug developments, the outcomes in the last two decades of the twentieth century were virtually identical to the first two decades; 30% or less recovered. The new medications are making a huge difference in people's lives, but they have side effects that are extremely distressing.

Why are we stuck? We have not been able to discover new targets for medications. We are using the same molecular targets, monoamine receptors and reuptake proteins. And we are focused on the same clinical targets: the Diagnostic and Statistical Manual (DSM) diagnostic entities. These targets limit development.

Static Molecular Targets Limit Drug Development

- Drug targets used in psychopharmacology have yielded many efficacious drugs, but
- Ultimately limited because based on existing drugs rather than pathophysiology
- Psychopharmacology needs valid, pathophysiologically relevant molecular targets

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Static Clinical Targets Limit New Drug Development

- DSM IV syndromes represent our current clinical targets
- Medicines treat symptoms, not DSM diagnoses
- Psychopharmacology needs new clinical targets closer to pathophysiology

NIMH

To address the need for new treatments, the National Advisory Mental Health Council has convened a treatment development workgroup chaired by Dennis Charney, M.D. The other members are Edward Scolnick, M.D., Jeffrey Lieberman, M.D., Charles Nemeroff, M.D., Larry Squire, Ph.D., Henry Lester, Ph.D., Jay McClelland, Ph.D., and Javier Escobar, M.D. Dr. Fenton will chair the Cognition/Schizophrenia subgroup; the depression subgroup chairs are Dennis Charney, M.D. and A. John Rush, M.D. The workgroup was formed in May 2001 and by September 2001 the Council had cleared three research concepts. In January 2002, a Request for Proposal (RFP) on cognition in schizophrenia was released (RFP number MH02DM0006). (The RFP is the first step in the letting of a contract.) In April 2002, a meeting on depression treatment was held. A schizophrenia treatment meeting took place in June.

Dr. Fenton told the Roundtable that the Institute can make a significant contribution. The public sector has specific competencies to exploit: discovering new molecular targets, new clinical targets and new clinical endpoints for treatment. NIMH can complement industry efforts by convening activities to develop targets and measurement tools, and by conducting basic science experiments to foster discovery, proof of concept trials and effectiveness studies.

There are scientific opportunities in depression research. Several new mechanisms are undergoing clinical testing: antagonists of substance P, antagonists of corticotropin releasing factor, melatonin receptor agonists and trace amine receptors.

In the area of measurement in affective disorders we have much work to do. Current methods yield approximately 50% placebo response rates. Clinical trial results cannot clearly indicate the superiority of the compound under trial compared to placebo. Current scales are not sensitive to novel mechanisms. NIMH and the measurement workgroup are examining a number of likely areas for progress.

Treatment development for cognitive impairment in schizophrenia has been hampered by lack of scientific consensus regarding both the key cognitive impairments to be targeted and the selection of reliable and valid measurement tools to assess cognition as a dependent variable in treatment trials. Given these limitations, the Food and Drug Administration (FDA) has not yet been able to recognize cognition in schizophrenia as a valid treatment endpoint for industry-sponsored research and drug registration. The RFP was designed to get at some of these issues.

Roundtable members had much to say about Dr. Fenton's talk. Particularly pointing out the great

need for new treatments and quickly. They greatly appreciated the Institute's efforts. New measures are desperately needed to maximize the possibility of learning from our research, particularly the "active agents" as compared to placebo. A Roundtable member suggested that NIMH keep its focus empirical and less theory driven and use basic psychological science measures. One person reminded the group that "symptoms are not equal to function." Reducing problematic symptoms does not necessarily improve functioning, and that is what matters. Another pointed out discrepancies in treatment application across specialties.

NIMH Services Research---Past, Present, Future

Junius J. Gonzales, M.D., Chief, Services Research and Clinical Epidemiology Branch, Division of Services and Intervention Research, NIMH



Dr. Gonzales told the Roundtable that NIMH services research is ultimately designed to improve mental health care for Americans. NIMH has played a central role in supporting the research that has contributed to the quality and breadth of treatments available and has reduced significantly the stigma attached to mental illnesses. The history of the field, however, contains disappointments. Scientific and clinical advances have helped the public to understand that mental illnesses are treatable medical conditions. However, many people are unable to obtain, for themselves or for one close to them, appropriate, state-of-the-art treatment for a mental illness. All too often, clinical practices and service system innovations that are validated by research are not fully adopted in treatment settings and service systems for individuals with mental illnesses. Dr. Gonzales said that the largest task facing mental health services research is determining the best ways to disseminate information. Right now we do not know if a person with a diagnosable mental illness will get the same treatment from a social worker in the District of Columbia, a psychiatrist in Maryland and a psychologist in Virginia. Cost and financing research in diverse populations of patients, providers, systems, and places -- "real world" ventures -- will help us get the answers we need.

In 1999, NIMH released a report by the National Advisory Mental Health Council's Clinical Treatment and Services Research Workgroup entitled *Bridging Science and Service*. This report contained 40 recommendations that have been partially or fully met. The NIMH definition of services research is: the multidisciplinary field of scientific investigation that studies how social factors, financing systems, organizational structures and processes, health technologies, and personal behaviors affect access to health care, the quality and cost of health care, and ultimately our health and well-being. Its research domains are individuals, families, organizations, institutions, communities and populations. The challenges, strengths, and promises include cost and financing issues, diverse populations (patients, providers, managed care, systems, states), "real world" settings, and high external validity and generalizability. This work also addresses limitations of traditional randomized clinical trials.

NIMH Services Research

- DSIR SRCEB
 - 10 programs; centers; training grants
 - Nearly 300 grants
 - 45% increase in applications from 2001->2002
 - www.nimh.nih.gov/srceb/index/cfm
- DMDBA
 - Center for AIDS: services component
 - Relevant Research Programs in Adherence, Stigma, Health Behavior



DSIR = Division of Services and Intervention Research
 SRCEB = Services Research and Clinical Epidemiology Branch
 DMDBA = Division of Mental Disorders, Behavioral Disorders and AIDS

Breadth of NIMH Services Research

• Child & Adolescent	• Sociocultural
• Primary Care	• Research Methods
• Quality of Care & Outcomes	• Clinical Epidemiology
• Financing & Managed Care	• Dissemination Research
• Systems Research	• Rural
	• Disablement & Functioning



The Services Research and Clinical Epidemiology Branch, of NIMH's Division of Services and Intervention Research, established a website to provide information on the NIMH programs. NIMH has been setting new standards for rigor and relevance with new grant mechanisms, interventions and practice research infrastructure development (R24), new 2001 division centers announcements integrating science and 'communities', network development, methods, and innovation, Time Sensitive Opportunities PA, Exploratory/Developmental R21, and the State Implementation RFA, which awards planning grants to states to study barriers to implementation.

Dr. Gonzales also told the Roundtable about an April 13 meeting entitled Evidence in Mental Health Services Research, What Types, How Much, and Then What? This research conference asked important questions related to evidence-based practice in order to tackle the challenges of weaving research, practice, and policy to improve care. The practice of medicine changes with or without a good science base, Dr. Gonzales said, referring attendees to a January 2002 editorial in the Journal of

the American Medical Association (JAMA) by Senator William H. Frist, M.D., "Federal Funding for Biomedical Research: Commitment and Benefits." Senator Frist calls for a greater emphasis on translating research discoveries into practice and the dissemination of these advances. The conference again drew attention to how difficult and complicated it is to move evidence into practice. Some concerns are increasing the capacity of the field and helping researchers to learn to work with scientists from unfamiliar disciplines, such as marketing and political science. It is crucial that we speed the transfer of research results to inform services. SAMHSA will no longer be conducting research. Although the funds formerly allocated to these projects at SAMHSA will not be transferred to NIMH, the Institute is interested in the portfolio and has been talking to SAMHSA about increasing linkages with them.

Dr. Gonzales told the group that the promise of health service research remains: to inform the provision of consistently provided quality care, across all settings, for all people who suffer from mental disorders, and their loved ones.

Open Discussion

Dr. Alan Kraut thanked Dr. Nakamura on behalf of the Roundtable for his visible, active leadership. He said that Dr. Nakamura had made himself easily accessible to advocates and scientists alike and was particularly grateful for new efforts toward training clinical psychologists.



Ms. Clarissa Wittenberg, NIMH Associate Director for Communications, announced a new advertising campaign addressed to men about depression. A series of spots will focus on men who have been successfully treated for depression, as it is more difficult to reach men with these messages.

During discussion concerning the value of longitudinal research, Dr. Nakamura discussed with Roundtable members the importance of moving beyond DALYs (Disability Adjusted Life Years). The Society for Social Work and Research partner suggested a rehabilitative approach that measures life course effects. Some of NIMH's services research focuses on long-term outcomes and it funds longitudinal studies in depression and schizophrenia, for instance.

In the wake of September 11th, NIMH is seeking a better understanding of the mental health consequences of trauma and terror. Dr. Nakamura said the Institute received and awarded a number of applications through the RAPID grants mechanism. It is not expected that these studies will lead to fundamentally new treatments, but they will analyze different populations and different exposures to the events. We are working with the Department to speed clinical trials, as we are on the verge of several medications to stop post-traumatic stress disorder.

Roundtable participants asked about the research emphasis on service delivery as it mediates treatment. There are many people in treatment outside the traditional mental health system, in jails, and the child welfare system for example. There is a need to create bridges. Dr. Gonzales said that NIMH is seeking the "active mechanism" what makes a treatment work. Providers are looking for faster, cheaper, and better treatments, and among the complex interventions being tested there is a need to distill the critical components.

A Parkinson's disease advocate highlighted a need to view services research and treatment development from the chronic disease standpoint. Assessing depression in people with other comorbid chronic illnesses is difficult as the symptoms overlap. NIMH staff stated that at this point the inclusive approach is probably better, looking at symptoms broadly, regardless of the underlying cause.

Another attendee asked about the development of research from cognition to emotion. Dr. Nakamura said that what we are learning about is how the genes and the circuitry interact. One of the most remarkable conclusions from recent research has been the plasticity of the brain. New neurons are growing, new synapses developing and new circuits being completed. The brain is not static. Individuals have some control over this brain construction to some extent. For example, how does exercise affect the brain? We are learning more and more about such things; but emotions, such as happiness are more elusive.

Gerald Weyrauch of the Suicide Prevention and Advocacy Network thanked Dr. Nakamura for his leadership and personal openness. Suicide is a fatal and near fatal consequence of mental illnesses. He suggested a national technical suicide information center to evaluate state programs. He saluted the Institutes' interaction with SAMHSA saying that such a partnership is essential. He asked how NIMH's Suicide Research Consortium takes advantage of research opportunities that arise. Dr. Jane Pearson is the consortium leader; she and staff members are working across the government to conduct appropriate studies.

In response to a question, Dr. Nakamura said that Dr. Steve Foote is leading the Institute's efforts in autism and attention deficit hyperactivity disorder (ADHD). NIMH is leading the Interagency Autism Coordinating Committee, which is the Federal Government-wide effort in autism. Reports of increases in the incidence of autism are alarming, however they may be due to changes in measurement. NIMH and the National Institute of Child Health and Human Development are leading the research activities at NIH and Members of Congress are very interested in these activities. With regard to ADHD, NIMH has long-term research ongoing. Stimulant medications are being prescribed earlier for children and we are looking at the safety and effectiveness of these medications in a variety of ages over time. Dr. Koretz said that the long-term findings are exciting and must now be translated into treatments and recommendations.

Another attendee expressed appreciation for the work NIMH is doing with the Child Abuse and Neglect Working Group; in particular the leadership of Dr. Cheryl Boyce.

David Helms, President and CEO of the Academy for Health Services Research said that NIMH "deserves a gold star" as its commitment to spending 15% of its budget for services research amounts to 25% of the entire NIH services research effort. He noted that NIMH is the biggest player in the field and he thanked Dr. Nakamura and Dr. Junius Gonzales for their leadership. Mr. Helms emphasized the importance of understanding of how services affect outcomes.

Another Roundtable member suggested the value of testing family functioning. Studies need to be designed in such a way that we can assess the "dose effect" of family structure and social supports. Dr. Nakamura said that racial and ethnic minority families often are the best examples of this effect and that NIMH would like to understand the phenomena. Good applications in this regard are necessary.

Dr. Nakamura also told the Roundtable that NIMH is working with the National Center for Complementary and Alternative Medicine to understand the placebo effect. What is it about patient

clinical interaction that affects recovery? How can we use the placebo effect to aid medication effects?

Another topic of discussion was the impact of marketing by pharmaceutical companies on the types of medications prescribed to patients. For example, lithium is not prescribed as often as Depakote because lithium has no advertising associated with it. These provider decisions are not based solely on the evidence base. NIMH should examine the issue of psychotropic prescribing and assess strategies for passing on what we know works best. Dr. Gonzales said that his division was about to fund a grant that will look at the impact of direct consumer advertising on prescribing. Again, Dr. Nakamura stressed the importance of finding the "active ingredients."

Ms. Lewis of the National Depression and Bipolar Support Alliance praised NIMH's willingness to collaborate, seeking advocates to help researchers. She said that she felt like she had an "equal seat." She suggested that more cross institute research, particularly with NIAAA and NIDA would allow NIMH to discover important information more quickly. Comorbidity is an area where collaboration is more difficult. NIMH is working with SAMHSA to evaluate integrated services, but problems arise on the local levels due to the separations in the funding streams.

Dr. Nakamura ended the meeting by reminding the Roundtable that NIMH "does not open its doors just once a year." He asked them to please come to staff and tell us what we can do better, how we can build quality and make significant improvements. Together we can make a difference.

Photos From the 2002 Roundtable



